REMARKS

At the outset, Applicants wish to thank Examiner Saunders for the courtesy extended to the undersigned and to Christine McCormack during a telephonic interview held on October 3, 2003. Applicants hereby amend the claims and present remarks consistent with the discussion therein.

Claims 1, 2, 4-8, 13, 24, 29, 34, 35 and 46-47 have been amended and claims 20-23, 42 and 44 have been cancelled. New claims 48-55 have been added. Upon entry of this paper, claims 1, 2, 4-8, 11-19, 24, 25, 29, 34-37 and 46-55 will be pending in the application.

Claim Amendments

The claims are amended to further clarify the claimed subject matter. Basis for the claim amendments can be found in the application, including the claims as originally filed.

Specifically, claim 1 has been amended to recite an antibody-based fusion protein which includes an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the C-terminal non-Ig protein comprising an amino acid alteration to a hydrophobic or non-polar amino acid within 10 amino acids of the N-terminus of the C-terminal non-Ig protein. Support for this amendment can be found in originally filed claims 1 and 45.

Claim 29 has been amended to recite that the fusion protein further comprises that the Ig chain includes an amino acid alteration to a hydrophobic or non-polar amino acid within the Ig chain. Support for this amendment can be found in the application as originally filed at least, for example, on page 3, lines 3-6.

Support for new claim 48 can be found in the application as originally filed at least, for example, on page 3, lines 3-6; on page 15, lines 11-12; and in originally filed claims 1 and 45.

Support for new claim 49 can be found in the application as originally filed at least, for example, on page 3, lines 3-6; on page 10, lines 10-18; on page 15, lines 11-12; and in originally filed claims 1 and 45.

Support for new claim 50 can be found in the application as originally filed at least, for example, on page 10, lines 10-18.

Support for new claim 51 can be found in the application as originally filed at least, for example, on page 3, lines 3-6 and lines 20-24 and in originally filed claims 1 and 45.

Support for new claim 52 can be found in the application as originally filed at least, for example, on page 15, lines 11-12.

Support for new claim 53 can be found in the application as originally filed at least, for example, in original claim 13. Support for new claims 53 and 54 can be found in the application as originally filed at least, for example, on page 3, lines 25-28; on page 10, lines 10-18; and on page 15, lines 11-12.

Support for new claim 55 can be found in the application as originally filed at least, for example, on page 5, lines 5-15.

Claims 2, 4, 7, 8, 13, 24, 25, 34, 46, and 47 have been amended to correct dependencies, claims 2 and 4-7 have been amended for consistency with antecedent claims and claim 35 has been amended to delete unnecessary words.

Applicants respectfully submit that the amendment does not introduce new matter and is made without any intention to abandon the subject matter as filed, but with the intention that claims of the same, greater, or lesser scope may be filed in a continuing application.

Claim Objections

The Office objects to claim 47 as being of improper dependent form. Applicants have amended claim 47 to correct its dependency and request reconsideration and withdrawal of the objection.

Claim Rejections Under 35 U.S.C. § 112, first paragraph

The Office rejected claims 1-2, 4-8, 11-19, 24-25, 29 and 34-37 under 35 U.S.C. §112, first paragraph. Specifically, the Office alleged that "Applicant's claims do not adequately describe the genus of fusion polypeptides, that have a longer circulating half-life."

In order to expedite prosecution, Applicants have amended claim 1 to include the limitation of claim 45. As amended, claim 1 specifically recites that the amino acid alteration includes altering an amino acid to a hydrophobic or non-polar amino acid. Applicants submit

that the subject matter of amended claim 1 is described in the Specification in such a way as to reasonably convey to one skilled in the art that Applicants were in possession of the claimed invention at the time the application was filed. See, for example, page 3, lines 25-28; page 9, lines 20-23 and Example 1 of the specification. Applicants respectfully submit that amended claim 1, all claims depending from claim 1, and new claims 48-55, comply with the requirements of 35 U.S.C. § 112, first paragraph. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim Rejections Under 35 U.S.C. § 112, second paragraph

The Office rejected claim 29 under 35 U.S.C. § 112, second paragraph. Specifically the Office stated that the use of "said first polypeptide" and "said second polypeptide" lack antecedent basis. Applicants have amended 29 to correct antecedent basis. In view of the amendment of claim 29, Applicants respectfully submit that claim 29 should no longer be rejected under 35 U.S.C. § 112, second paragraph, and respectfully request reconsideration and withdrawal of the rejection.

Claim Rejections Under 35 U.S.C. § 102

The Office rejected claim 1 as anticipated under 35 U.S.C. § 102 over Gillies *et al.* (WO 99/43713; referred to herein as "Gillies *et al.*"). Specifically, the Office alleged that "Gillies *et al.* teach that the serum half-life may be extended and the FcR binding activity reduced by substituting a C.gamma.4 region in lieu of a C.gamma.1 region (page 2, lines 21+ and Example 1). Inspection of Fig. 2B shows that a C.gamma.4 region differs from a C.gamma.1 region by an amino acid substitution at position 442, which is within 10 residues of the C-terminal end thereof." Applicants traverse this rejection as maintained against the amended claims.

Anticipation under 35 U.S.C. §102 requires that all of the elements and limitations of the claim(s) at issue be found within a single prior art reference. Carella v. Starlight Archery and Pro Line Co., 804 F.2d 135, 231 USPQ 644 (Fed. Cir. 1986). In order to anticipate a claim, the identical invention must be shown in as complete detail as is contained in the patent claim.

Richardson v. Suzuki Motor Co., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989); (M.P.E.P. §2131.01).

Applicants submit that amended claim 1 is not anticipated by Gillies *et al.* As amended, claim 1 is directed to an antibody-based fusion protein which includes an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the C-terminal non-Ig protein comprising an amino acid alteration to a hydrophobic or non-polar amino acid within 10 amino acids of the N-terminus of the C-terminal non-Ig protein. Gillies *et al.* do not teach an antibody-based fusion protein where an amino acid in the non-Ig protein is altered to a hydrophobic or non-polar amino acid. Accordingly, Applicants submit Gillies *et al.* cannot anticipate claim 1 and respectfully request reconsideration and withdrawal of the rejection.

Applicants further submit that new independent claims 48, 49 and 51 are also not anticipated under 35 U.S.C. § 102 over Gillies *et al.*

Applicants submit that new claim 48 is not anticipated by Gillies *et al.* New claim 48 is directed to an antibody-based fusion protein which includes an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, wherein the Ig chain is an IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE chain comprising an amino acid alteration to a hydrophobic or non-polar amino acid within ten amino acids from the C-terminus of the Ig chain. As noted in the Office action Gillies *et al.* teach substituting a C.gamma.4 region for a C.gamma.1 region. Gillies *et al.*, however, do not teach an IgG1 chain comprising an amino acid alteration to a hydrophobic or non-polar amino acid within ten amino acids of its C-terminus, do not teach an IgG4 chain comprising an amino acid alteration to a hydrophobic or non-polar amino acid within ten amino acids of its C-terminus and do not teach an IgG2, IgG3, IgA, IgM, IgD, or IgE chain comprising an amino acid alteration to hydrophobic or non-polar amino acid within ten amino acids of its C-terminus. Applicants therefore submit that new claim 48 is not anticipated by Gillies *et al.*

Applicants submit that new claim 49 is not anticipated by Gillies *et al.* New claim 49 is directed to an antibody-based fusion protein comprising an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the Ig chain comprising an IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE constant domain and an amino acid alteration to a hydrophobic or non-polar amino acid within 10 amino acids from its C-terminus of the Ig chain. Gillies *et al.* do not

teach an Ig-based fusion protein having an an IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE constant domain where the Ig constant chain includes an amino acid alteration to a hydrophobic or non-polar amino acid within 10 amino acids from its C-terminus of the Ig chain as required by new claim 49. Applicants therefore submit that new claim 49 is not anticipated by Gillies *et al.*

Applicants submit that new claim 51 is not anticipated by Gillies *et al.* New claim 51 recites an antibody-based fusion protein including an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein, the Ig chain including an amino acid sequence that is non-natural within 10 amino acids from its C-terminus, the non-natural amino acid sequence including an amino acid alteration to a hydrophobic or non-polar amino acid. Since Gillies *et al.* do not teach an Ig chain having a non-natural amino acid residue within 10 amino acids from its C-terminus, Applicants submit that Gillies *et al.* do not anticipate new claim 51.

Claim Rejections Under 35 U.S.C. § 103

The Office rejected Claims 1-2, 5-8, 11-19, 24-25, 34-35, and 45-46 under 35 U.S.C. § 103(a) as unpatentable over Gillies *et al.* in view of Chang *et al.* (U.S. Patent No. 5,908,626 or 5,723,125; referred to herein as the '626 patent and the '125 patent).

The present invention relates to an antibody-based fusion protein which includes an N-terminal Ig chain linked to a C-terminal non-Ig protein having any of the following modifications:

(i) an amino acid alteration to a hydrophobic or non-polar amino acid within 10 amino acids of the N-terminus of the C-terminal non-Ig protein (as recited in amended claim 1);

(ii) an amino acid alteration to a hydrophobic or non-polar amino acid within 10 amino acids from the C-terminus of an IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE chain (as recited in new claim 48);

(iii) an amino acid alteration to a hydrophobic or non-polar amino acid within 10 amino acids from the C-terminus of the Ig chain, wherein the Ig chain includes a IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE constant domain (as recited in new claim 49); or

(iv) an amino acid sequence that is non-natural within 10 amino acids from the C-terminus of the Ig chain and the non-natural amino acid sequence includes an amino acid

alteration to a hydrophobic or non-polar amino acid (as recited in new claim 51). The claimed antibody-based fusion protein with these modifications have a longer circulating half-life *in vivo* than a corresponding unmodified antibody-based fusion protein.

The antibody-based fusion proteins of the present invention are not suggested by Gillies *et al.*, by Chang *et al.*, or by their combination.

Gillies *et al.* do not teach or suggest that altering an amino acid residue in the non-Ig protein or in the Ig chain of IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE to a hydrophobic or non-polar amino acid sequence near the junction area between the Ig and the non-Ig chains will result in the fusion protein having a longer circulating half life. Moreover, Gillies *et al.* do not teach or suggest making alterations within 10 amino acids from the C-terminus of the N-terminal Ig chain and/or within 10 amino acids from the N-terminus of the C-terminal non-Ig protein, as recited in amended claim 1 and new claims 48, 49 and 51.

The failure of Gillies *et al.* to suggest the present invention is not remedied by the '626 patent or the '125 patent of Chang *et al.* The '125 and '626 patents do not disclose or suggest an antibody-based fusion protein having a configuration as claimed in the present invention, *i.e.*, an N-terminal immunoglobulin (Ig) chain linked to a C-terminal non-Ig protein. Moreover, the '125 and '626 patents do not disclose or suggest:

(i) an amino acid alteration to a hydrophobic or non-polar amino acid within 10 amino acids of the N-terminus of the C-terminal non-Ig protein (as recited in amended claim 1);

(ii) an amino acid alteration to a hydrophobic or non-polar amino acid within 10 amino acids from its C-terminus of an IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE chain (as recited in new claim 48);

(iii) an amino acid alteration to a hydrophobic or non-polar amino acid within 10 amino acids from its C-terminus of the Ig chain, wherein the Ig chain includes a IgG1, IgG2, IgG3, IgG4, IgA, IgM, IgD, or IgE constant domain (as recited in new claim 49); or

(iv) an amino acid sequence that is non-natural within 10 amino acids from its C-terminus of the Ig chain and the non-natural amino acid sequence includes an amino acid alteration to a hydrophobic or non-polar amino acid (as recited in new claim 51).

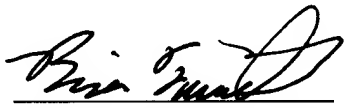
Finally, the '125 and '626 patents provide no reasonable expectation that such an antibody-based fusion protein would have a longer circulating half-life *in vivo* than a corresponding antibody-based fusion protein without the amino acid alteration.

Applicants therefore respectfully request that all the rejections under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

CONCLUSION

Applicants submit that on the basis of the foregoing remarks and claim amendments, claims 1, 2, 4-8, 11-19, 24, 25, 29, 34-37 and 45-54 are in condition for immediate allowance. Accordingly, Applicants respectfully request entry as such.

Respectfully submitted,



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